

Extended Summary

SCI Pesticides Group and RSC Meeting: Natural Products as a Source of Crop Protection Agents III

The following is an extended summary based on a paper presented at the meeting 'Natural Products as a Source of Crop Protection Agents III' organised by L. G. Copping, B. P. S. Khambay and A. Mudd on behalf of the SCI Pesticides Group and the Royal Society of Chemistry and held at 14/15 Belgrave Square, London, on 9 & 10 December 1996.

Biologically Active Compounds from Marine Organisms

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Serious consideration of marine organisms as sources of biologically active compounds has been restricted to the last 40 years or so. However, during this period, numerous novel compounds have been isolated from marine organisms and many of these substances have been demonstrated to possess interesting biological activities. The range of compounds can be appreciated from the regular reviews by Faulkner (Reference 1 and earlier cited references). The examples quoted in this brief summary will concentrate on compounds with potential pharmaceutical and agricultural uses.

Drugs active against human viruses are in great demand and many marine organisms have been screened for the presence of compounds with antiviral activity. This work has been intensified as a result of the worldwide AIDS epidemic. Avarol (Fig. 1; **1**) and avarone (**2**), extracted from the sponge *Disidea avara* have been reported to inhibit immunodeficiency virus, have high therapeutic indices and the ability to cross the blood–brain barrier. These compounds have, therefore, potential use in the treatment of AIDS.² However, the only substance reported to have any significant therapeutic activity is ara-A (**3**), which is a semi-synthetic substance based on the arabinosyl nucleosides from the sponge *Tethya crypta*.

Many marine organisms have been tested in the search for compounds with potential for development as anti-cancer drugs. The best known are the macrolides

known as bryostatins, for example bryostatin-1 (**4**), which have been isolated primarily from the bryozoan, *Bugula neritina*. These compounds stimulate human haemopoietic cells, and thus the bryostatins have been suggested for the treatment of neoplastic bone-marrow-failure states.³ Cell growth inhibitory activity *in vitro* has been demonstrated by dolastatins, a group of cyclic and linear peptides and depsipeptides isolated from the sea hare, *Dolabella auriculata* (for example, dolastatin-10) (**5**).⁴

Marine plants and animals have been investigated as sources of antiparasitic compounds. α -Kainic acid (**6**), isolated from the red alga *Digenia simplex*, is marketed as a broad-spectrum anthelmintic. It is effective against the parasitic round worm, the whip worm and the tape worm. A chemically related compound, domoic acid (**7**), also has anthelmintic properties. This has been isolated from the red algae *Chondria armata* and *Alsidium coral-linum* and also, more recently, from species of diatoms. Ingestion of shellfish contaminated with these domoic-acid-containing diatoms has led to cases of human poisoning, including several fatalities. The toxic effects produced are known as amnesic shellfish poisoning.⁵

Many compounds isolated from marine organisms have been shown to have antimicrobial properties. The best known is perhaps cephalosporin C (**8**), isolated from the fungus *Cephalosporium acremonium*. A semi-synthetic derivative of this compound, cephalothin sodium, is a widely-used antibiotic drug.⁶ Istamycins A (**9**) and B (**10**) are further examples of antibiotic substances isolated from marine micro-organisms. These compounds, produced by fermentation using *Streptomyces tenjimariensis* SS-939, have activity against both Gram-positive and Gram-negative bacteria, including those with known resistance to the aminoglycoside antibiotics.⁷

Other significant properties reported for compounds

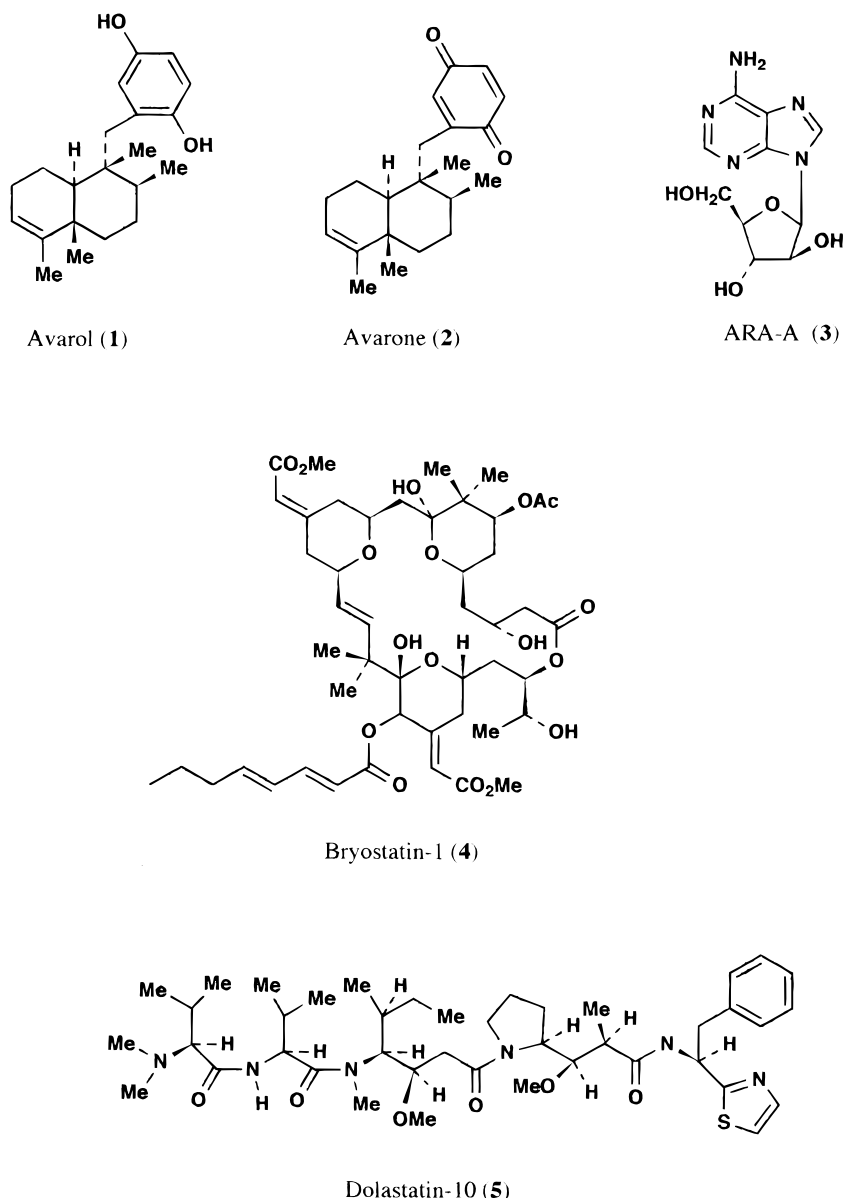


Fig. 1. Biologically active compounds from marine organisms.

isolated from marine organisms include anti-inflammatory and anticoagulant activities. One of the bi-indoles (**11**) isolated from the cyanobacterium, *Rivularia firma*, is active in both the carrageenan-induced rat paw oedema and kaolin rat paw oedema tests, which are routine procedures used for screening for anti-inflammatory activity.⁸ The anticoagulant properties recorded are associated with sulphated polysaccharides isolated from marine algae.

Marine organisms have also been screened for substances with potential agrochemical use. The annelid, *Lumbriconeris heteropoda*, has long been known to be active against insects. The active compound, nereistoxin (**12**), has rapid anaesthetic effects on insects and is toxic to fish and mammals. Studies on this substance led to the introduction of the synthetic pesticide cartap.⁹

Extracts and suspensions of brown algae are used in agriculture and horticulture and many different effects have been reported as a result of their use, including increased crop yields, increased resistance of treated plants to stress conditions, increased uptake of nutrients, reduced storage losses of fruit and vegetables and improved seed germination.¹⁰ The active compounds present in the extracts have not been fully elucidated, but recent studies have implicated betaines, such as glycinebetaine (**13**), γ -aminobutyric acid betaine (**14**) and δ -aminovaleric acid betaine (**15**). There have been several reports which show that the application of seaweed extracts to plants resulted in decreased incidence of nematode attack. For example, Whapham *et al.*¹¹ reported that the use of an alkaline extract of *Ascophyllum nodosum* as a root drench resulted in sig-

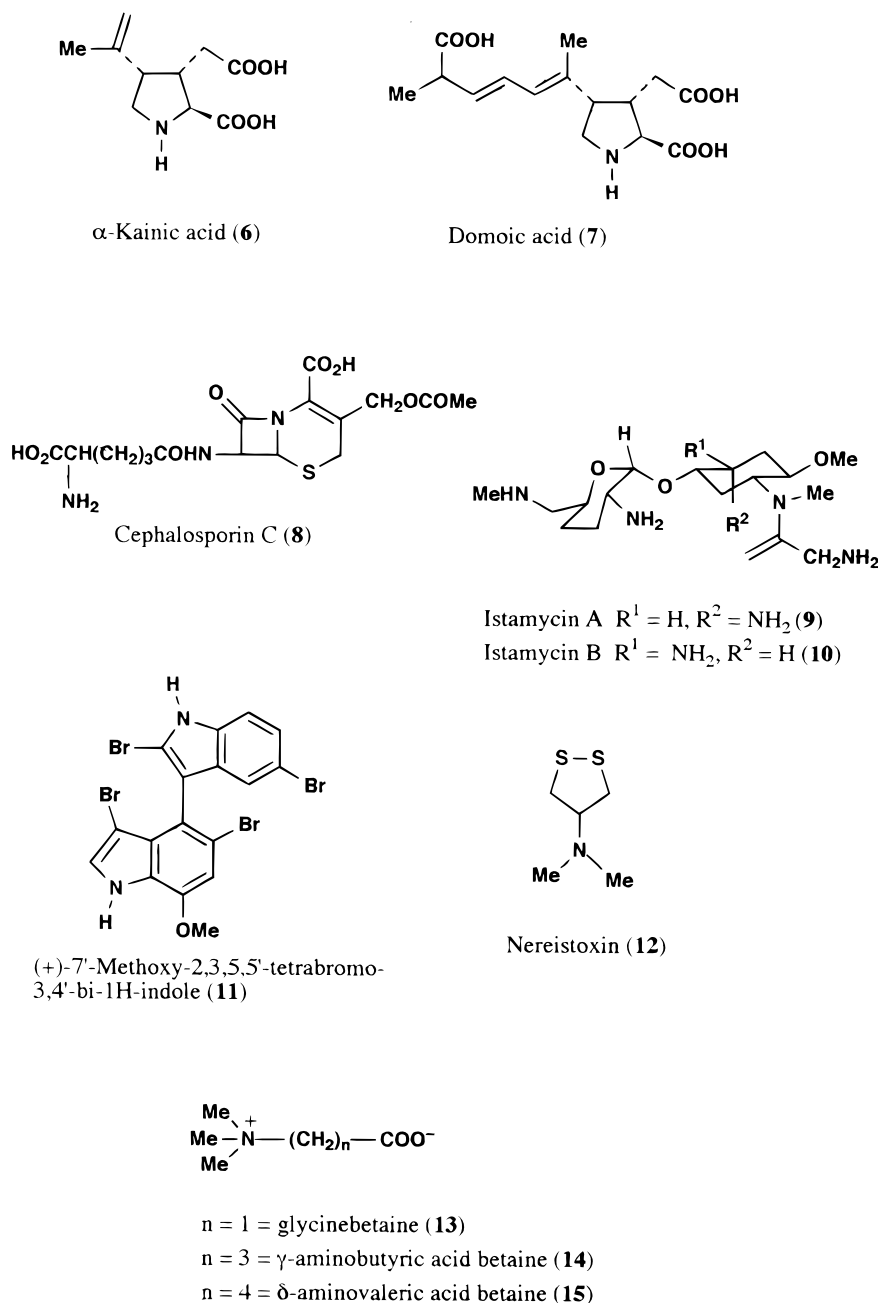


Fig. 1. (Continued)

nificantly reduced numbers of *Meloidogyne javanica* eggs recovered after one generation from the roots of tomato plants. Further study showed that use of the extract also produced a significant reduction in the number of second-stage juveniles of both *M. javanica* and *M. incognita* invading the roots. Egg recovery from the seaweed-extract-treated plants was also significantly lower. The three major betaines found in the seaweed extract, when applied in amounts equal to those in the extract, also led to significant reductions in both the nematode invasion profile and egg recovery.¹²

Seaweed extract when applied to either the soil or to the foliage of tomato plants was reported to result in the treated plants having greener leaves.¹³ Repetition of

this experiment using seaweed extract and an equivalent quantity of the betaines found in the extract resulted in significantly enhanced leaf chlorophyll levels with both treatments in tomato, dwarf French bean, wheat and barley.¹⁴

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